REMARKS

Claims 27 and 29-32 are all the claims pending in the application; claims 31 and 32 are withdrawn from consideration; claims 27, 29 and 30 are rejected.

I. Rejection of Claims Under 35 U.S.C. §103

A. At paragraph 6 of the Office Action, claims 27, 29 and 30 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,171,799 in view of Schwarz et al. (1995) and Jones et al. (1992).

The Examiner states that the '799 patent teaches a culture device for culturing immunosuppressive (suppressor) cells, with an affinity for protein, wherein prior to culturing, the culture device is coated with an anti-CD3 antibody (OKT3). The Examiner admits that the disclosure of the '799 patent differs from the claimed invention in that it does not teach a device further coated with an $F(ab)_2$ fragment of the anti-CD2 antibody TS2/18 antibody produced by the hybridoma HB195.

With regard to Schwarz et al., the Examiner states that this reference teaches the culture of T cells with the anti-CD2 TS2/18 antibody, resulting in inhibitory effects on T cell activation, and that the epitope recognized by TS2/18 is a candidate for CD2-directed immunosuppression.

The Examiner goes on to explain that Jones et al. teaches the interchangeability of whole antibodies and $F(ab)_2$ fragments for the coating of devices (plastic plates) for the incubation of lymphocytes, and that the $F(ab)_2$ fragment may be preferable.

The Examiner concludes that it would have been obvious to make a culture device pre-coated with anti-CD3 antibodies as taught by the '799 patent, and also coated by an anti-CD2

TS2/18 antibody, as taught by Schwarz et al., using either whole antibody or an $F(ab)_2$ fragment, as taught by Jones et al.

The Examiner states that the motivation for preparing such a device, double-coated with anti-CD2 and anti-CD3 antibodies, is because such a device should achieve additional immunosuppression of the immunosuppressive (suppressor) T cells.

In response, Applicants note that the present invention relates to a culture device for inducing activation of immunosuppressive cells, wherein the culture device comprises a container coated with the $F(ab)_2$ fragment of the anti-CD2 antibody TS2/18 produced by hybridoma HB195, and at least one anti-CD3 antibody.

In contrast to the Examiner's position, Applicants assert that none of the references cited by the Examiner teach or suggest the combination of a container comprising the $F(ab)_2$ fragment of the anti-CD2 antibody TS2/18 and an anti-CD3 antibody, for use in inducing activation of immunosuppressive cells.

USSN 6,171,799 only discloses a culture device coated with an anti-CD3 antibody.

Schwartz et al. only discloses that the full-size anti-CD2 antibody TS2/18 inhibits T cell activation.

As to Jones et al., this reference only discloses that false-positive reactions due to non-specific interference rarely occurred when $F(ab')_2$ antibody fragments were used, as compared to intact antibodies (see, e.g., Abstract lines 4-6, and page 234, column 1, lines 17-27) in assays for IFN-γ in the plasma of cattle. Although the Examiner states that "whole antibodies and $F(ab)_2$ fragments are interchangeable and in some situations an $F(ab)_2$ fragment is preferable, as taught by Jones et al." (page 3, lines 18-20, of the Office Action), there is neither a description nor a

suggestion regarding inducing activation of immunosuppressive cells. Therefore, because the technical field of Jones et al. is different from that of the present invention (i.e., an enzyme immunoassay versus the induction of activation of immunosuppressive cells), Jones et al. would not have motivated the skilled artisan to use the $F(ab)_2$ fragment in place of the anti-CD2 antibody TS2/18 in the culture device of Schwartz et al., neither for the more effective induction of activation of immunosuppressive cells or any other purpose. Thus, there would have been no motivation to combine the teachings of Jones et al. with any of the other cited references.

Thus, even if one were motivated to combine the disclosures of the '799 patent and Schwarz et al. and produce a device coated with the TS2/18 antibody and an anti-CD3 antibody, one of ordinary skill in the art would not have further combined the disclosure of Jones et al., to arrive at Applicants' invention (using the $F(ab)_2$ fragment).

In addition to the points above, Applicants contend that the culture dishes of the present invention show unexpectedly superior results compared to those of the cited references. As disclosed in Test Example 1 of the instant application (pages 18-19), the immunosuppressive effects of the devices coated only with the $(Fab)_2$ fragment of the anti-CD2 antibody TS2/18 (example 1(c)), coated only with an anti-CD3 antibody (example 1(d)), or coated with both the anti-CD2 antibody TS2/18 and an anti-CD3 (example 1(e)), are 20%, 50% and 67% suppression, respectively. In contrast, the immunosuppressive effect of the device coated with both the $F(ab)_2$ fragment of the TS2/18 antibody and an anti-CD3 antibody (example 1(f)) (as presently claimed) is 78% suppression. Even in view of the references cited by the Examiner, the greater suppressive effect seen with the $F(ab)_2$ fragment of the TS2/18 antibody and an anti-CD3 antibody was unexpectedly superior.

Thus, as there would have been no motivation to combine the references cited by the Examiner to arrive at the presently claimed invention, and in view of the unexpectedly superior results, Applicants respectfully assert that the invention as presently claimed would not have been obvious to one of ordinary skill in the art at the time of the invention over the references cited by the Examiner. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At paragraph 7 of the Office Action, claims 27, 29 and 30 are also rejected under 35 U.S.C. §103(a) as being unpatentable over EP 0 421 380 (1990) in view of Schwarz et al. (1995) and Jones et al. (1992).

The Examiner states that the '380 application teaches a culture device coated with an anti-CD3 antibody and an anti-CD2 antibody, including an enzymatically cleaved antibody fragment. The Examiner admits that the disclosure of the '380 application differs from the claimed invention in that it does not teach the specific anti-CD2 antibody TS2/18 produced by the hybridoma HB195 nor the use of an $F(ab)_2$ fragment.

With regard to Schwarz et al., the Examiner states that this reference teaches the well-known anti-CD2 TS2/18 antibody produced by the hybridoma HB195.

The Examiner goes on to explain that Jones et al. teaches the interchangeability of whole antibodies and $F(ab)_2$ fragments for the coating of devices (plastic plates) for the incubation of lymphocytes, and that the $F(ab)_2$ fragment may be preferable.

The Examiner concludes that it would have been obvious to make a culture device coated with anti-CD3 antibodies and an anti-CD2 antibody as taught by the '380 application, using the anti-CD2 TS2/18 antibody of Schwarz et al., using either whole antibody or an $F(ab)_2$ fragment,

as taught by Jones et al., given the fact that whole antibodies and $F(ab)_2$ fragments are interchangeable and in some cases, $F(ab)_2$ fragments are preferable.

In response, Applicants respectfully assert that one of ordinary skill in the art, at the time Applicants produced their invention, would not have been motivated to combine the three references cited by the Examiner to arrive at the present invention.

As discussed under section **A.** above, Applicants assert that none of the references cited by the Examiner teach or suggest the combination of a container comprising the $F(ab)_2$ fragment of the anti-CD2 antibody TS2/18 and an anti-CD3 antibody, for use in inducing activation of immunosuppressive cells.

The '380 application only discloses a culture device comprising an anti-CD2 antibody and an anti-CD3 antibody for inducing tumor-lysing cells.

Schwartz et al. only discloses that the full-size anti-CD2 antibody TS2/18 inhibits T cell activation.

As discussed above, Jones et al. does not teach the interchangeability of whole antibodies and $F(ab)_2$ fragments, nor a preference for using the $F(ab)_2$ fragment, for inducing activation of immunosuppressive cells.

As also discussed above, the culture dishes of the present invention show unexpectedly superior results compared to those of the cited references.

Because there would have been no motivation to combine the references cited by the Examiner to arrive at the presently claimed invention, and in view of the unexpectedly superior results, Applicants respectfully assert that the invention as presently claimed would not have been obvious to one of ordinary skill in the art at the time of the invention over the references

cited by the Examiner. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

II. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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